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Health Effects Assessment for Barium

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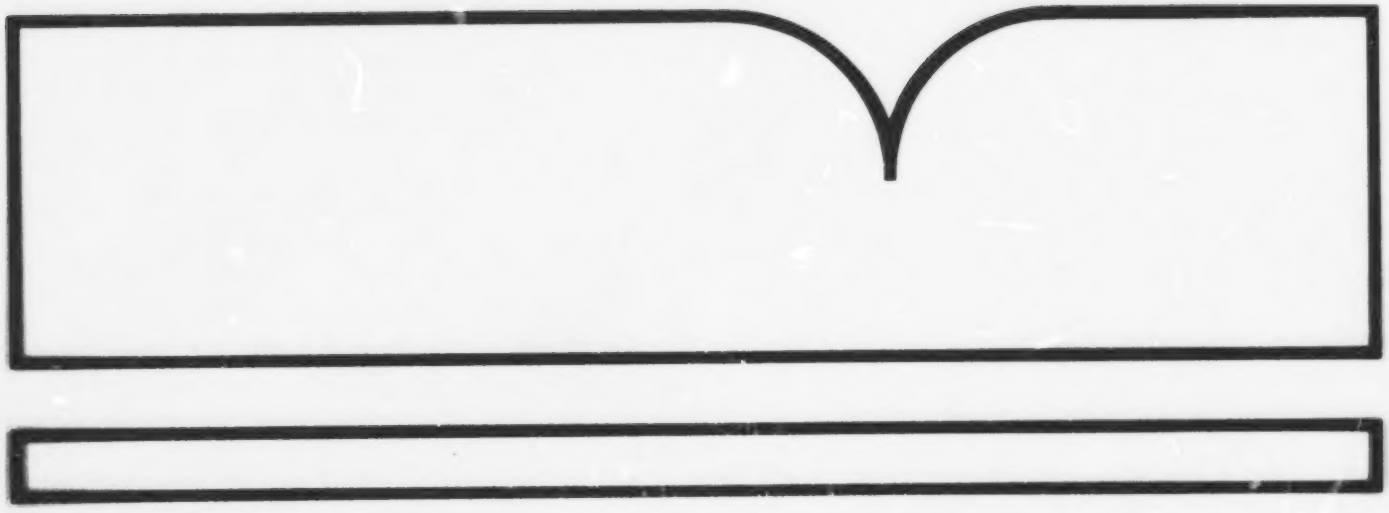

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HEALTH EFFECTS ASSESSMENT FOR BARIUM

U.S. Environmental Protection Agency
Office of Research and Development
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Cincinnati, OH 45268

U.S. Environmental Protection Agency
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Office of Solid Waste and Emergency Response
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16. ABSTRACT

This document represents a brief, quantitatively oriented scientific summary of health effects data. It was developed by the Environmental Criteria and Assessment Office to assist the Office of Emergency and Remedial Response in establishing chemical-specific health-related goals of remedial actions. If applicable, chemical-specific subchronic and chronic toxicity interim acceptable intakes are determined for systemic toxicants, or q_1^* values are determined for carcinogens for both oral and inhalation routes.

A chronic interim acceptable intake was determined for barium based on oral exposure and both a subchronic and chronic interim acceptable intake was determined based on inhalation exposure.

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PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with barium. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the Chemical Abstracts, TOXLINE, CANCERLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to September, 1984. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1980b. Mini-Reviews on the Carcinogenicity, Mutagenicity, Teratogenicity and Chronic Toxicity of Selected Compounds. Environmental Criteria and Assessment Office, Cincinnati, OH. Internal draft.

U.S. EPA. 1983b. Reportable Quantity for Barium. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, the AIS or acceptable intake subchronic, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for AIS estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure.

The AIC, acceptable intake chronic, is similar in concept to the ADI (acceptable daily intake). It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980a) for a discussion of this concept]. The AIC is route specific and estimates acceptable exposure for a given route with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for ranking reportable quantities; the methodology for their development is explained in U.S. EPA (1983a).

For compounds for which there is sufficient evidence of carcinogenicity, AIS and AIC values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980a). Since cancer is a process that is not characterized by a threshold, <u>any</u> exposure contributes an increment of risk. Consequently, derivation of AIS and AIC values would be inappropriate. For carcinogens, q_1^*s have been computed based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, refer to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates presented.

An oral AIC of 3.6 mg/day has been estimated for barium based on a LOAEL of 100 mg Ba/ℓ in drinking water. This estimate is based primarily on a rat study showing an increase in systolic blood pressure following consumption of water containing 100 mg Ba/ℓ. The data used for this estimate are limited and new data should be evaluated when available. Data were inadequate for development for estimation of an oral AIS for barium.

A CS of 45 was associated with shortened lifespan in male mice treated with Ba^{+2} in the drinking water.

An AIS and AIC for inhalation exposure have been estimated as 0.098 and 0.01 mg/day, respectively. These estimates are based on an animal study showing reproductive effects in rats following exposure to 3.62 mg Ba/m³. Appropriate human data addressing reproductive issues are not available. Corroborating animal studies are also unavailable. The data base for these estimates is considered extremely limited. The AIC is well below the recommended TLV for occupational exposures, reflecting concern for potential reproductive effects.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
bw	Body weight
CAS	Chemical Abstract Service
CNS	Central nervous system
CS	Composite score
DNA	Deoxyribonucleic acid
GI	Gastrointestinal
LOAEL	Lowest-observed-adverse-effect level
MED	Minimum effective dose
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase
TLV	Threshold limit value

1. ENVIRONMENTAL CHEMISTRY AND FATE

Barium is an alkaline-earth metal belonging to Group IIA of the periodic table. Elemental barium has a CAS Registry number of 7440-39-2. The inorganic chemistry of barium consists exclusively of compounds in the 2^+ valence state. Selected physical properties of a few environmentally significant barium compounds are given in Table 1-1.

The following discussion of the fate and transport of barium in various environmental media is speculative and is based on analogy to the environmental behavior of other metals and the known chemical properties of barium and its compounds.

The physical sources of atmospheric barium are probably industrial emissions. Barium is likely to be present in particulate form in the atmosphere. Although chemical reactions may cause speciation of the chemical in air, the main mechanisms for the removal of barium compounds in the atmosphere are likely to be wet precipitation and dry deposition. The residence time of barium in the atmosphere may be several days, depending on the particulate size and the chemical nature of the particulate.

In aquatic media, barium is likely to be present primarily as suspended particulate matter or sediments. The soluble form of barium in most aquatic systems may be controlled by the solubility product of barium carbonate. In the absence of any other possible removal mechanisms, the residence time of barium in aquatic systems could be several hundred years.

In soils, barium is not expected to be very mobile because of its formation of water-insoluble salts and its inability to form soluble complexes with humic and fulvic materials. Under acidic conditions, however, some of the water insoluble barium compounds may become soluble and move back into groundwater.

TABLE 1-1

Selected Physical Properties of a Few Barium Compounds[a]

Element/ Compound	Formula	Atomic/ Molecular Weight	Specific Gravity/ Density	Water Solubility	Vapor Pressure (mm Hg)
Barium	Ba	137.34	3.51 g/cm³ at 20°C	decomposes	10 mm at 1049°C
Barium carbonate	$BaCO_3$	197.35	4.43	2 mg/100 mℓ[b] at 20°C	NA
Barium chloride	$BaCl_2$	208.25	3.856 g/cm³ at 24°C	37.5 g/100 mℓ[b] at 26°C	NA
Barium oxide	BaO	153.34	5.72	3.48 g/100 mℓ at 20°C	NA
Barium sulfide	BaS	169.40	4.25 g/cm³ at 15°C	decomposes	NA
Barium sulfate	$BaSO_4$	233.40	4.50 g/cm³ at 15°C	0.222 mg/100 mℓ at 18°C	NA

[a]Source: Weast, 1980

[b]These data are for the alpha-isomer

NA = Not available

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

Pertinent data regarding the absorption of barium from the GI tract were not located in the available literature. Systemic toxic effects have been observed following oral exposure, implying that some absorption does occur. McCauley and Washington (1983) studied the absorption of various barium salts and reported relative absorption rates of barium chloride > barium sulfate > barium carbonate.

2.2. INHALATION

Pertinent data regarding the absorption of barium from the respiratory tract were not located in the available literature. Systemic toxicity has been observed following inhalation exposure, implying that some absorption does occur. Gore and Patrick (1982) found that, in rats, intratracheally administered barium sulfate was concentrated in the area immediately beneath the basement membrane within 24 hours and remained in this area for at least 7 days.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

3.1.1. Oral. Tardiff et al. (1980) administered drinking water containing 0, 10, 50 or 250 mg Ba^{++}/ℓ (as barium chloride) to groups of 30 Charles River rats of both sexes for 4, 8 or 13 weeks. The authors reported that these concentrations corresponded to doses of 0, 1.7, 8.1 or 38.1 mg Ba/kg bw/day for males and 0, 2.1, 9.7 or 45.7 mg Ba/kg bw/day for females. The diet supplied ~0.5 µg Ba/kg bw/day. There were significant decreases in the relative weights of the adrenals in males in the 50 and 250 mg/ℓ groups after 8 weeks, but not after 13 weeks, and in the females in the 250 mg/ℓ group only after 13 weeks. Relative adrenal weights also appeared lower in the 10 and 50 mg/ℓ females, but these decreases were not statistically significant. Relative adrenal weights were higher in the 250 ppm females after 8 weeks. The significance of these findings is uncertain since a clear dose effect or dose duration pattern does not emerge. The authors state that the differences in adrenal weights did not appear to be dose related. No adverse effects were observed with respect to food consumption, body weight, clinical signs, mortality, hemoglobin levels, hematocrit, red cell count, leukocyte count, prothrombin time, fibrinogen, serum enzyme activities (SGOT, SGPT), blood urea nitrogen, serum sodium, potassium or calcium, gross pathology, or histopathology.

3.1.2. Inhalation. Tarasenko et al. (1977) investigated the effects of inhalation exposure to barium (as barium carbonate dust) on the general health and reproductive function in male and female rats. Unspecified numbers of male rats were exposed to $BaCO_3$ dust at levels of 5.2 and 1.15 mg/m³, 4 hours/day for 6 months. The animals in the high-dose group had decreased body weight, changes in hematologic parameters, decreased clearance times for bromosulphthalein by the liver, and other "general toxic

effects." The low-dose animals had no observed effects resulting from the exposure. In the reproductive toxicity evaluation an atmospheric concentration of 22.6 mg $BaCO_3/m^3$ resulted in decreased numbers of spermatozoids and a lower percentage of motile sperm forms in male rats exposed for one cycle of spermatogenesis (daily duration of exposure not reported). Exposure of females to 13.4 mg $BaCO_3/m^3$ for 4 months (daily duration of exposure not reported) resulted in increased mortality in subsequent litters and a general underdevelopment of the newborn pups. No systemic effects were reported for the female rats exposed to 3.1 mg $BaCO_3/m^3$, but this exposure level did produce some ovarian follicle atresia. Exposure of males to an atmospheric concentration of 5.2 mg $BaCO_3/m^3$, 4 hours/day for 4 months resulted in increased mortality of fetuses following mating of treated males with untreated females.

3.2. CHRONIC

3.2.1. Oral. U.S. EPA (1985) presented a complete review of Perry et al. (1983) with the addition of added experimental details obtained from the authors. The following synopsis of Perry et al. (1983) is taken primarily from U.S. EPA (1985). Perry et al. (1983) exposed female weanling Long-Evans rats to 1, 10 or 100 ppm barium (administered as $BaCl_2$) in drinking water for up to 16 months. Average daily doses of 0.051, 0.51 and 5.1 mg/kg bw/day were calculated by U.S. EPA (1985) based on water consumption data. Weight and systolic pressure measurements were made at 1, 2, 4, 8, 12 and 16 months. Each exposure group contained 12-13 animals and each exposure period had 21 control animals. There were no significant differences in growth rate, water consumption or food consumption, and no gross signs of toxicity when barium groups were compared with control groups.

Animals exposed to 1 ppm barium for 1-16 months showed no changes in average systolic blood pressure. Animals exposed to 10 ppm barium showed small but significant ($p<0.01$) increases in mean systolic blood pressure of 6, 7 and 4 mm Hg over controls after 8, 12 and 16 months, respectively. The 100 ppm barium-exposed animals had significant increases in mean systolic pressures ($p<0.001$) which averaged 12, 16 and 16 mm Hg after 1, 12 and 16 months, respectively. Heart physiology and biochemistry was evaluated only in the 100 ppm barium-exposed animals at 16 months. These animals showed depressed rates of cardiac contraction and depressed electrical excitability. In addition, cardiac ATP, phosphocreatine and phosphorylation potential were decreased and ADP was increased.

U.S. EPA (1985) considered the increases in systolic blood pressure seen following exposure to 10 ppm to be not large enough to constitute an adverse health effect and designated the associated dose, 0.51 mg/kg bw/day, a NOAEL. U.S. EPA (1985) designated the dose associated with the 100 ppm barium exposure, 5.1 mg/kg/day, a LOAEL. U.S. EPA (1985) also pointed out that the basal level of other trace metals, particularly calcium, supplied to animals throughout the study may have contributed to the toxicity of barium.

Brenniman et al. (1979a,b, 1981) investigated the relationship between barium concentrations in the drinking water and increased blood pressure and mortality in several communities in Illinois. These communities were divided into high-exposure ($\geq$2.0-10 mg Ba/ℓ) and low-exposure (<0.2 mg Ba/ℓ) populations. Communities with populations >2500 in the 1970 census were chosen for comparison. The high-exposure communities (total population = 25,433) had an average of 7 mg Ba/ℓ in their drinking water, and the low-exposure communities (total population = 46,905) had an average of

0.1 mg Ba/ℓ. For comparison of blood pressures, 1000 individuals (age ≥18) from each community were tested. Mortality data were obtained from death certificates. No significant differences in blood pressure were observed. The significantly increased death rate among males and females combined was due to "all cardiovascular diseases," "heart disease" and "all causes." When analyzed separately, the only statistically significant differences were an increase in deaths from "all cardiovascular diseases" in males and from "all causes" in females. The authors pointed out the following confounding factors to be considered in the evaluation of their results: 1) inability to control for use of home water softeners, 2) movement in and out of the community, 3) high variability in barium well water concentrations.

Schroeder and Mitchener (1975a) administered barium acetate at a level of 5 mg Ba/ℓ in the drinking water to Long-Evans rats for their lifetimes. Both the control and treated groups consisted of 52 male and 52 female animals. The authors considered the slight changes observed, growth rate (increased in older females), longevity (insignificant decrease in the mean of the last surviving 10% in both males and females), gross pathology and histopathology, to have no biologic significance.

In a comparison study, Schroeder and Mitchener (1975b) administered drinking water containing barium acetate (5 mg Ba/ℓ) to groups of 42 male and 36 female Swiss mice for their lifetimes. Controls consisted of 54 mice of each sex. No effect was observed on body weight, gross pathology or histopathology. Longevity, defined as the mean age at death of the last surviving 10% of animals, was slightly reduced ($p<0.025$) in the treated males (815 days vs. 920 days for controls), but the average age at death did not differ between the treated (548 days) and control (540 days) males.

3.2.2. Inhalation. Pertinent data regarding the chronic inhalation toxicity of barium were not located in the available literature.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

3.3.1. Oral. Pertinent data regarding the teratogenicity or other reproductive effects of orally administered barium in humans or experimental animals were not located in the available literature.

3.3.2. Inhalation. Pertinent data regarding the teratogenicity of inhaled barium in humans or experimental animals were not located in the available literature. Data relating to reproductive function in experimental animals have been included in Section 3.1.2.

3.4. TOXICANT INTERACTIONS

The toxic effects of barium result largely from an increase in muscle excitability, particularly cardiac muscle; effects on the hematopoietic system; and effects on the CNS (ACGIH, 1980). Welch et al. (1983) reported that the antinociceptive and lethal effects of barium chloride could be reversed by naloxone or atropine. Naloxone was more effective in blocking the antinociceptive effects and atropine was a more effective antagonist for the lethal effects.

4. CARCINOGENICITY

4.1. HUMAN DATA

Pertinent data regarding the potential carcinogenicity of barium to humans following either oral or inhalation exposure were not located in the available literature.

4.2. BIOASSAYS

4.2.1. Oral. Schroeder and Mitchener (1975a,b) investigated the carcinogenicity of barium acetate administered in the drinking water to both rats and mice. In both studies, animals (52 rats/sex/group and 42-54 mice/sex/group) were maintained on drinking water containing 5 mg Ba/ℓ for their lifetimes. The incidence of gross total tumors and malignant tumors in male rats were, respectively, 4/26 (15%) and 2/26 (8%) in controls, and 8/30 (26%) and 6/30 (20%) in the treated animals. In female rats, the respective incidences were 17/24 (70%) and 8/24 (33%) in controls, and 15/30 (45%) and 9/33 (27%) in the treated animals. The observed differences in tumor incidence were not statistically significant. In mice, the incidences of multiple tumors, lymphoma leukemia, lung tumors and total tumors were nearly identical in the treated and control groups.

4.2.2. Inhalation. Pertinent data regarding the carcinogenicity of inhaled barium were not located in the available literature.

4.3. OTHER RELEVANT DATA

Nishioka (1975) reported that barium chloride produced no increased mutation frequency in repair deficient strains of Bacillus subtilis. Negative results have were obtained in tests for the induction of errors in viral DNA transcription in vitro (Loeb et al., 1978).

4.4. WEIGHT OF EVIDENCE

IARC has not evaluated the risk of humans associated with oral or inhalation exposure to barium. Using the criteria for evaluating the overall weight of evidence of carcinogenicity to humans proposed by the Carcinogen Assessment Group of the U.S. EPA (Federal Register, 1984), barium is most appropriately designated a Group D chemical - not classified. No data are available regarding the carcinogenicity of barium to humans. Although barium was not apparently carcinogenic to rats and mice in the Schroeder and Mitchener (1975a,b) bioassays, only one dosage level was used which elicited few toxic effects and was apparently not near the acceptable intakes.

5. REGULATORY STANDARDS AND CRITERIA

The ACGIH (1980, 1983) has proposed a TLV of 0.5 mg/m^3, based on the results of Hyatt (1980), who had employed this limit for several years at the Los Alamos Laboratories with satisfactory results for the control of exposure to barium nitrate. All jurisdictions that have adopted limits for barium compounds have accepted the TLV of 0.5 mg/m^3 (ACGIH, 1980).

6. RISK ASSESSMENT

6.1. ACCEPTABLE INTAKE SUBCHRONIC (AIS)

6.1.1. Oral. Only one study on the effects of subchronic oral administration of barium was found in the available literature. Tardiff et al. (1980) reported decreased relative adrenal weights in male rats receiving doses as low as 8.1 mg Ba/kg bw/day for 8 weeks; however, there were no differences after 13 weeks. Female relative adrenal weights appeared to be depressed after 13 weeks exposure to 45.7 mg/kg/day. As discussed in Section 3.1.1., the significance of these findings is uncertain. For risk assessment purposes, these data appear to represent a free-standing NOAEL and therefore are inadequate for estimation of an AIS. In Section 6.2.1. on chronic toxicity, adequate data are available.

6.1.2. Inhalation. The only study pertinent to the subchronic inhalation toxicity of barium is that of Tarasenko et al. (1977). Exposure of male rats to atmospheric concentrations of 3.62 mg Ba/m³ (5.2 mg $BaCO_3$/m³), 4 hours/day, for 4 months resulted in "general" signs of toxicity that included decreased body weight and liver function and increased mortality of fetuses following mating of treated males with untreated females. An exposure to 0.80 mg Ba/m³ (1.15 mg $BaCO_3$/m³) resulted in no observed toxic effects in the adult males; however, effects on reproductive performance were not reported for this dose group. The exposure level of 0.80 mg Ba/m³ is a NOEL. Assuming a breathing volume of 0.26 m³/day for rats, and multiplying by 4 hours/24 hours to represent continuous exposure, this exposure corresponds to a dose of 0.035 mg Ba/day or 0.14 mg Ba/kg bw/day (average weight of 0.246 kg). Applying an uncertainty factor of 100, 10 for interspecies conversion and 10 to allow for the most sensitive members of the population, results in an AIS of 0.0014 mg Ba/kg bw/day or 0.098 mg Ba/day for a 70 kg human.

6.2. ACCEPTABLE INTAKE CHRONIC (AIC)

6.2.1. Oral. Two studies contained data useful for establishing a threshold for toxicity from chronic oral exposure to barium. Brenniman et al. (1979a,b) reported a significant increase in death from "total cardiovascular diseases" in communities whose water supply contained an average of 7 mg Ba/ℓ, compared with communities whose water supply contained an average of 0.1 mg Ba/ℓ. However, as noted previously a number of confounding factors limit the usefulness of this study.

U.S. EPA (1985) utilized the 16-month LOAEL of 5.1 mg/kg/day defined by Perry et al. (1983) in a study where barium was administered to rats in the drinking water as the basis for an ADI estimate. They applied an uncertainty factor of 100 (10 for interspecies extrapolation and 10 for inter-individual variability). An additional uncertainty factor to estimate a NOAEL from a LOAEL was not considered appropriate because

> "...a major limitation of this study [Perry et al., 1983] is the minimized exposure to trace metals (e.g., Ca) in the food, water and laboratory environment, and this may have contributed to the observed effects. To accomodate for this, the EPA feels that selection of an uncertainty factor of 100 is more appropriate."

Using the LOAEL of 5.1 mg/kg/day, multiplying by 70 kg and dividing by 100 resulted in an ADI of 3.6 mg/day. This ADI may serve as an AIC estimate until additional data concerning the toxicology of barium are available.

A CS for slightly reduced longevity in male mice exposed to drinking water containing Ba^{+2} at 5 ppm in the Schroeder and Mitchener (1975b) experiment was calculated. Assuming that mice drink water equivalent to 17% of their body weight/day, the animal dose is 0.85 mg Ba^{+2}/kg/day. The corresponding human MED was derived by multiplying the animal dose by the cube root of the ratio of the body weight of mice (0.04 kg approximated from

data provided) to that of humans (assumed to be 70 kg). The result, 0.07 mg/kg/day, multiplied by 70 kg yields a human MED of 4.9 mg/day, corresponding to an RV_d of 4.5. An RV_e of 10 is appropriately applied to the effect of reduced longevity. A CS of 45, the product of RV_d and RV_e, results.

6.2.2. Inhalation. Pertinent data regarding the chronic inhalation toxicity of barium were not located in the available literature. A TLV for barium of 0.5 mg/m³ has been in effect for several years with no reported adverse effects. Assuming an average workday breathing volume of 10 m³ and multiplying by 5/7 to convert from 5-day to 7-day exposures result in an estimated NOEL of 3.57 mg/day. As can be readily seen, however, this value is higher than the subchronic NOEL defined by animal studies. Two strategies are feasible. One could assume that the animal extrapolation results in an overly conservative AIS and adjust the AIS upward based on the TLV. Alternatively, the AIS could be adjusted downward. Adverse reproductive outcomes have been reported in animal studies with $BaCO_3$ at 3.62 mg Ba/m³. These types of effects are difficult to detect in the human population and probably would not be apparent in exposed workers even if present, unless careful epidemiological investigations designed to evaluate these endpoints were conducted. In view of this, it is recommended that the AIS for inhalation of 0.098 mg/day be adopted as a chronic interim ADI with an additional uncertainty factor of 10. This results in a suggested AIC of 0.01 mg barium/day. This estimate should be carefully reevaluated when more complete reproduction data are available.

6.3. CARCINOGENIC POTENCY (q_1^*)

Pertinent data regarding a carcinogenic potential for barium following either oral or inhalation exposure were not located in the available literature. Therefore, no q_1^* could be derived.

7. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. Cincinnati, OH. p. 35. (Cited in U.S. EPA, 1983b)

ACGIH (American Conference of Governmental Industrial Hygienists). 1983. Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom with Intended Changes for 1983-1984. Cincinnati, OH.

Brenniman, G., W. Kojola, P. Levy, B. Carnow and T. Namekata. 1979a. Health Effects of Human Exposure to Barium in Drinking Water. NTIS PB 292268. (Cited in U.S. EPA, 1980b)

Brenniman, G.R., T. Namekata, W.H. Kojola, B.W. Carnow and P.S. Levy. 1979b. Cardiovascular disease death rates in communities with elevated levels of barium in drinking water. Environ. Res. 20: 318-324.

Brenniman, G.R., W.H. Kojola, P.S. Levy, B.W. Carnow and T. Namekata. 1981. High barium levels in public drinking water and its association with elevated blood pressure. Arch. Environ. Health. 36: 28-32.

Federal Register. 1984. Environmental Protection Agency. Proposed guidelines for carcinogenic risk assessment. Federal Register. 49: 46204-46299.

Gore, D.J. and G. Patrick. 1982. A quantitative study of the penetration of insoluble particles into the tissue of the conducting airways. Ann. Occup. Hyg. 26(1-4): 149-161. (CA 98:30673n)

Hyatt, E.C. 1980. Communication to TLV Committee member. (Cited in ACGIH, 1980)

Loeb, L., M. Sirover and S. Agarwal. 1978. Infidelity of DNA synthesis as related to mutagenesis and carcinogenesis. Adv. Exp. Med. Biol. 91: 103-115. (Cited in U.S. EPA, 1980b)

McCauley, P.T. and I.S. Washington. 1983. Barium bioavailability as the chloride, sulfate or carbonate salt in the rat. Drug Chem. Toxicol. 6(2): 209-217. (CA 99:17715d)

Nishioka, H. 1975. Mutagenic activities of metal compounds in bacteria. Mutat. Res. 31: 185-189. (Cited in U.S. EPA, 1980b)

Perry, H.M., E.F. Perry, M.N. Erlanger and S.J. Kopp. 1983. Cardiovascular effects of chronic barium ingestion. In: Proc. 17th Ann. Conf. Trace Substances in Environmental Health, Vol. 17. Univ. of Missouri Press, Columbia, MO. p. 155-164.

Schroeder, H. and M. Mitchener. 1975a. Life-term studies in rats: Effects of aluminum, barium, beryllium and tungsten. J. Nutr. 105: 421-427.

Schroeder, H. and M. Mitchener. 1975b. Life-term effects of mercury, methyl mercury and nine other trace metals on mice. J. Nutr. 105: 452-458. (Cited in U.S. EPA, 1980b, 1983b)

Tarasenko, M., O. Promin and A. Silayev. 1977. Barium compounds as industrial poisons (an experimental study). J. Hyg. Epidem. Microbiol. Immunol. 21: 361. (Cited in U.S. EPA, 1980b)

Tardiff, R.G., M. Robinson and N.S. Ulmer. 1980. Subchronic oral toxicity of barium chloride in rats. J. Environ. Pathol. Toxicol. 4: 267-275. (Cited in U.S. EPA, 1983b)

U.S. EPA. 1980a. Guidelines and Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Quality Criteria. Federal Register. 45: 79347-79357.

U.S. EPA. 1980b. Mini-Reviews on the Carcinogenicity, Mutagenicity, Teratogenicity and Chronic Toxicity of Selected Compounds. Environmental Criteria and Assessment Office, Cincinnati, OH. Internal draft.

U.S. EPA. 1983a. Methodology and Guidelines for Reportable Quantity Determinations Based on Chronic Toxicity Data. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983b. Reportable Quantity for Barium. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH, OHEA for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1985. Drinking Water Criteria Document for Barium. Office of Drinking Water, Washington, DC. External Review Draft.

Welch, S.P., F.J. Vocci and W.L. Dewey. 1983. Antinociceptive and lethal effects of intraventricularly administered barium and strontium: Antagonism by atropine sulfate or naloxone hydrochloride. Life Sci. 33(4): 359-364.

Weast, R.C., Ed. 1980. CRC Handbook of Chemistry and Physics, 61st ed. CRC Press, Boca Raton, FL. p. B80-B81; D-199.

APPENDIX

Summary Table for Barium

	Species	Experimental Dose/Exposure	Effect	Acceptable Intake (AIS or AIC)	Reference
Inhalation					
AIS	rat	0.8 mg Ba/m^3	NOEL	0.098 mg/day	Tarasenko et al., 1977
AIC	human	0.5 mg/m^3	NOEL based subchronic study	0.01 mg/day	Tarasenko et al., 1977
Oral					
AIS				ND	
AIC	rat	100 ppm Ba drinking water	LOAEL for increased blood pressure	3.6 mg/day	Perry et al., 1983
Maximum composite score	mice	100 ppm Ba^{+2} in drinking water for 16 months (RV_d = 2.8)	Increased blood pressure (RV_e = 7)	19.6	Schroeder and Mitchener, 1975b; U.S. EPA, 1983b

ND = Not derived